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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,774	03/13/2003	Tracey Brown	DACO:002US	2305
7590	05/19/2004		EXAMINER	
Steven L Highlander Fulbright & Joworski 600 Congress Avenue Suite 2400 Austin, TX 78701			BERKO, RETFORD O	
			ART UNIT	PAPER NUMBER
			1615	
DATE MAILED: 05/19/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,774	BROWN ET AL.	
	Examiner	Art Unit	
	Retford Berko	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 17 February 2004.
 2a) This action is **FINAL**. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 13-50 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 13-50 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>5/15/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Acknowledgement: Applicant's Amendment filed February 17, 2004 is acknowledged.

Status of Claims

1. The status of the claims is as follows:
 - (a) Claims 1-13 are cancelled in view of applicant's preliminary amendment filed March 13, 2004.
 - (b) Claims 13-50 are added in preliminary amendment filed March 13, 2004 and subject of the first office action.
2. Claims 13-50 are currently pending.

Claim Rejections - 35 USC § 112

3. Claims 13-24 remain rejected under 35 USC 112, first paragraph. The scope of the claims is interpreted as preventing metastases of cancer by administering effective amount of hyaluroran. Giving the broadest interpretation to the claims, it is the examiner's position that the claims are directed toward the prevention of cancer from invading a particular area. The evidence submitted is insufficient and there is no statistical data supporting the prevention of cancer evidenced in the broad scope of the claims. While hyaluroran may be effective in sensitizing non-lymphoid tumor cells to certain antineoplastic agents in vitro and therefore may be useful in treatment of lymphatic cancer, at best such evidence is only a single example of the effectiveness of hyalurolan in cancer treatment and is not supportive of the broad concept of cancer prevention. Secondly, there is no declaration on file showing evidence of the effectiveness of hyaluoran as effective antineoplastic agent in vivo. The examiner intepretes the

data in examples 2, 4 and Figure 6 as being inadequate to permit broad interpretation that hyaluroran is effective in the prevention of cancer in a subject including a mammal.

Claim Rejections-35 USC 102

4. The rejection of claims 13-19, 23-30 and 34-35 under 35 USC 102(b) as being anticipated by both Sakura et al ([Sho 61 (6191986)-17 and Faulk et al (WO 95/30423) is withdrawn in view of applicant's amendment.

Claim Rejections- 35 USC 103

5. Claims 20-21, 31-33 and 50 remain rejected under 35 USC 103(a) as being unpatentable over Harper et al (US 5, 977, 088) in view of Faulk et al (US 5, 827, 834).

Response To Arguments

6. Applicant's arguments filed February 9, 2004 have been fully considered but they are found not persuasive.

7. Applicant argues that specification does indeed support the use of hyaluroran to prevent metastasis (Example 4 and Fig. 6), that mice treated with hyalurolan showed a significant reduction in lymphoid metastasis, as compared to controls.

8. In response to this argument, Example 4 (Spec at page 38) shows the effect of hyalurolan on the in vitro efficacy of -FU to inhibit proliferation of cancer cells. Figure 6 shows the effect of hyaluronan and 5-FU in combination to inhibit metastasis in lymphoid tissue. The evidence is only a single example of the effectiveness of hyalurolan in enhancing the antineoplastic effect and reduction of metastasis and the usefulness for treatment of cancer in lymphoid tissue. However, the evidence is insufficient to support the generic claim—ie the effectiveness of hyalurolan in preventing cancer metastasis. Moreover, the prior art (Sakura et al ([Sho 61

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(6191986)-17) discloses the cancer metastasis inhibitory effects of hyalurolan and cross-linked hyalurolan in mice.

9. Applicant argues that Sakura et al does not disclose a method in which metastasis is prevented, that the disclosure at most suggests a method and that the working examples of the reference do not support the methodology. Applicant contends that Sakura et al indicates hyalurolan inhibits binding of cells to tissue, renders the cells anchorage independent and thereby promotes metastasis.

10. In response, Sakura et al discloses that hyaluronic acid reduces bonding ability of tumor cells (page 16) and reduces the number of metastatic foci in lung in murine model (page 19). Applicant's contention of the likelihood that hyalurolan inhibits binding of tumor cells to tissue, rendering the cells anchorage independent and thus likely promoting metastasis is not disclosed in the prior art reference.

11. Applicant argues that by amending claims 13 and 25 to recite a hyaluronan of molecular weight 750, 000 daltons which is not taught in the prior art cited, the rejection of the claims under 35 USC 103 over Harper et al (US 5, 977, 088) in view of Faulk et al (US 5, 827, 834) should be withdrawn, that there is no basis for combining the two references as they use hyaluronic acid for different purposes and that the use of hyaluronic acid having molecular weight of less than 750, 000 daltons is inconsistent with the claims that are drawn toward the use of hyaluronic acid of greater molecular weight.

12. In response to this argument, Patent '088 discloses that hyaluronic acid facilitates or causes the transport of medicine and/or therapeutic agent into the skin to the site of pathology and/or trauma (col 9, lin 60-65), providing the motivation to combine hyalurolan with other

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therapeutic agents in order to effect treatment due to increased bioavailability of drug to sites.

Also, because the prior art discloses the use of hyaluronic acid in the composition, the burden shifts on applicant to show that molecular weight of the compound as claimed is critical.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is 571-272-0590. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

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applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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